REMARKS

This amendment responds to the office action mailed February 25, 2003. Claims 1-17 were pending in the instant Application. With the instant amendment, claims 10-17 have been canceled, without prejudice, as drawn to non-elected subject matter. Claims 1-9 have been canceled, without prejudice, and replaced by new claims 18-46. Thus, after entry of the instant amendment, claims 18-46 are pending and under consideration. New claims 18-46 are fully supported by the specification and the claims as originally filed. Support for new claims 18-24 can be found in the specification, at, for example, page 109 (Example 19), in Figure 10 and in claims 1-2, 4-6 and 8-9, respectively, as originally filed. Support for new claims 25-46 can be found in the specification, at, for example, pages 12-19, Examples 3-18 and Figures 4-9B.

Applicant expressly reserves the right to pursue any canceled subject matter in one or more related, continuation, divisional or continuation-in-part application(s).

I. THE REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

A. The Rejection of Claims 1-9

Claims 1-9 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. As pointed out, above, none of claims 1-9 are currently pending. However, for the reasons set forth below, Applicant asserts that the pending claims are definite under 35 U.S.C. §112, second paragraph.

The PTO bases its rejection of claims 1-9 on the contention that the claims fail to identify the mutation(s) that correlates with the desired phenotype. (Office Action, p. 3). Specifically, the claims are rejected because the PTO contends that the claims fail to identify the precise mutation that is being detected. *Id.* The PTO further contends that the claims refer to an HIV integrase and an HIV-infected patient, without identifying whether the HIV virus is HIV-1 or HIV-2. *Id.* Specifically, the PTO states that "clearly setting forth the virus (*e.g.*, HIV-1 or HIV-2) and codon (*e.g.*, 66) are important to understanding the invention, . . . and absent further clarification and amendment of the claim language, the metes and bounds of the patent protection desired cannot be ascertained." *Id.*

The new claims are definite and particularly point out that which Applicant has always considered the claimed subject matter. In particular, in the method recited in each of

the pending claims it is explicitly indicated that the patient is an HIV-1-infected patient and that the mutation is detected at codon 66 in HIV-1 integrase. Applicant respectfully submits that the pending claims clearly set forth the virus (*i.e.*, HIV-1) and the codon (*i.e.*, codon 66) as recommended by the PTO. As such, the above-summarized concern with respect to claims 1-9 is not relevant to the definiteness of the pending claims and Applicant respectfully requests that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

B. The Rejection of Claims 1-4 and 9

Claims 1-4 and 9 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. As pointed out, above, none of claims 1-4 or 9 are currently pending. However, for the reasons set forth below, Applicant asserts that the pending claims are definite under 35 U.S.C. §112, second paragraph.

The PTO bases its rejection on the contention that "NNRTIs . . . target the HIV-1 reverse transcriptase (RT), not the integrase (IN). Thus it is not readily manifest how the detection of a genotypic change in the IN would correlate to an RT phenotype." (Office Action, p. 3).

The pending claims are definite and particularly point out and distinctly define the metes and bounds of the subject matter that the Applicant has always considered as the invention. "Whether a claim is invalid for indefiniteness requires a determination whether those skilled in the art would understand what is claimed when the claim is read in light of the specification. *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993). Applicant submits that one of skill in the art would understand the pending claims when read in light of the specification. In particular, the method of independent claim 18 is directed to a method of assessing the effectiveness of antiretroviral therapy on an HIV-1-infected patient by detecting, in a biological sample of the HIV-1-infected patient, the presence of a nucleic acid that exhibits a mutation at codon 66 of a nucleotide sequence encoding HIV-1 integrase, wherein the presence of such a mutation correlates with an increase in susceptibility to delavirdine, nevirapine, or efavirenz.

The pending claims clearly recite a correlation between a mutation at codon 66 of a nucleotide sequence encoding HIV-1 integrase and an increase in susceptibility to delavirdine, nevirapine, or efavirenz. The specification, at page 109-110, demonstrates this correlation. Whether this result is surprising, or whether the mechanism underlying this

result is evident, is not relevant to the patentability of the claims under 35 U.S.C. § 112, second paragraph. Further, as discussed in the next section, the specification clearly describes the claimed matter so as to enable one of skill in the art to make and/or use the invention.

II. THE REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH, (ENABLEMENT) SHOULD BE WITHDRAWN

A. The Rejection of Claims 1-4 and 9

Claims 1-4 and 9 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being not enabled. As pointed out, above, none of claims 1-4 or 9 are currently pending. However, for the reasons set forth below, Applicant asserts that the pending claims are fully enabled under 35 U.S.C. §112, first paragraph.

The PTO bases its rejection of claims 1-4 and 9 on the contention that "the disclosure fails to provide a correlation between NNRTI -resistance and genotypic changes in the IN." (Office Action, p. 4). Specifically, the claims are rejected because the PTO contends that "NNRTIs . . . do not target the IN but are specific for the RT. Thus, genotypic changes in the IN *would not be expected* to correlate with NNRTI-drug susceptibility." *Id.* (emphasis added). Expected or not, Applicant respectfully notes that the specification clearly demonstrates the correlation between genotypic changes in HIV-1 integrase and NNRTI susceptibility.

The new claims are fully enabled by the specification as originally filed and merely clarify that which Applicant has always considered the claimed subject matter. As stated above, the method of independent claim 18 is directed to a method of assessing the effectiveness of antiretroviral therapy on an HIV-1-infected patient by detecting, in a biological sample of the HIV-1-infected patient, the presence of a nucleic acid that exhibits a mutation at codon 66 of a nucleotide sequence encoding HIV-1 integrase, wherein the presence of such a mutation correlates with an increase in susceptibility to delavirdine, nevirapine, or efavirenz.

The enablement requirement requires a determination "of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation." *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990); *see also*

Genentech, Inc. v. Novo Nordisk, 108 F.3d 1361, 1365 (Fed. Cir. 1997); *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991).

At page 109 (Example 19) of the instant application, Applicant describes the construction of a resistance test vector comprising a mutation at codon 66 of the HIV-1 integrase protein and its use in a phenotypic assay to determine susceptibility to various NNRTIs, for example, delavirdine, nevirapine and efavirenz, and to integrase inhibitors, for example, L-731,988. The example discloses that the presence of a mutation at codon 66 of the HIV-1 integrase protein results in increased susceptibility to nevirapine, delavirdine and efavirenz, but decreased susceptibility to L-731,988. The actual increase or decrease observed is plotted on a graph and the graphs (one for each of the drugs studied) is presented in Figure 10 (page 110). The graphs show an increased susceptibility for NVP, DLV and EFV, but a decreased susceptibility for L-731,988. Applicant therefore submits, that contrary to the PTO's allegations, the specification does teach a correlation between NVP, DLV and EFV susceptibility and genotypic changes at codon 66. Accordingly, Applicant submits that one of skill in the art, guided by the specification, would be fully enabled to practice the full scope of the methods recited in the pending claims.

Applicant reminds the PTO that an inventor need not comprehend the scientific principles behind the invention. *Cross v. Iizuka*, 753 F.2d 1040 (Fed. Cir. 1985). It is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works. *Id.; see also Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570 (Fed. Cir. 1983); *In re Cortright*, 165 F.3d 1353 (Fed. Cir. 1999). Furthermore, statements that a physiological phenomenon was observed are not inherently suspect because the underlying basis for the observation cannot be predicted or explained. *In re Cortright*, 165 F.3d 1353. Applicant therefore submits that the PTO's conclusion that the claims are not enabled just because NVP, DLV and EFV are *conventionally* known to target HIV-1 reverse transcriptase, lacks merit.

Moreover, if a patent discloses a single working embodiment in a predictable art, the courts have consistently held that the patent is enabled. *See, e.g., Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533 (Fed. Cir. 1987); see also *Gould v. Mossinghoff*, 711 F.2d 396, 400 (D.C. Cir. 1983). Applicant therefore submits that the specification, for example, the working example on page 109 (Example 19) and the graphs of Figure 10 fully enable one of skill in the art to assess the effectiveness of antiretroviral therapy on an HIV-1-infected patient by detecting, in a biological sample of the HIV-1-infected patient, the

presence of a nucleic acid that exhibits a mutation at codon 66 of a nucleotide sequence encoding HIV-1 integrase, wherein the presence of such a mutation correlates with an increase in susceptibility to delavirdine, nevirapine, or efavirenz without undue experimentation. Other working examples and figures, *e.g.*, Examples 3-18 and Figures 4-9 enable one of skill in the art to further assess the effectiveness of antiretroviral therapy on an HIV-1-infected patient by detecting whether a nucleic acid that exhibits mutations in a nucleotide sequence encoding HIV-1 reverse transcriptase is present in the biological sample of the HIV-1-infected patient, wherein the presence of the mutation correlates with a change in susceptibility to various NNRTIs.

As such, the above-summarized concern with respect to claims 1-4 or 9 is not relevant to the enablement of the subject matter recited in the pending claims. Applicant submits that one of skill in the art, guided by the specification, would be fully enabled to practice the full scope of the methods recited in the pending claims.

B. <u>The Rejection of Claims 5-8</u>

Claims 5-8 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being not enabled. As pointed out, above, none of claims 5-8 are currently pending. However, for the reasons set forth below, Applicant asserts that pending claims 21-23, supported by original claims 5-7, are fully enabled under 35 U.S.C. §112, first paragraph.

The PTO bases its rejection of claims 5-8 on the contention that "the claims are broadly directed toward phenotypic screening methods by assessing the presence or absence of a mutation at codon 66 of the HIV IN." (Office Action, p. 4).

New claims 21-23 are fully enabled by the specification as originally filed and merely clarify that which Applicant has always considered the claimed subject matter. In particular, the methods of claims 21-23 are directed to a method of assessing the effectiveness of antiretroviral therapy on an HIV-1-infected patient by detecting, in a biological sample of the HIV-1-infected patient, the presence of a nucleic acid that exhibits a mutation at codon 66 of a nucleotide sequence encoding HIV-1 integrase, wherein the presence of such a mutation correlates with a decrease in susceptibility to L-731,988.

As discussed above, the enablement requirement requires a determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation.

At page 109 (Example 19) of the instant application, Applicant describes the construction of a resistance test vector comprising a mutation at codon 66 of the HIV-1 integrase protein and its use in a phenotypic assay to determine susceptibility to integrase inhibitors, for example, L-731,988. The example discloses that the presence of a mutation at codon 66 of the HIV-1 integrase protein results in decreased susceptibility to L-731,988. This observed decrease in susceptibility is plotted on a graph and is presented in Figure 10 (page 110). The graph shows a decreased susceptibility for L-731,988. Applicant submits that one of skill in the art, guided by the specification, would be fully enabled to practice the full scope of the methods recited in new claims 21-23.

As such, the above-summarized concern with respect to claims 5-8 is not relevant to the enablement of the subject matter recited in the pending claims. Applicant submits that one of skill in the art, guided by the specification, would be fully enabled to practice the full scope of the methods recited in amended claims 21-23.

CONCLUSION

In light of the above amendments and remarks, Applicant respectfully submits that claims 18-46 satisfy all the criteria for patentability and are in condition for allowance. Applicant requests that the Examiner reconsider this application with a view towards allowance and solicit an early passage of claims 18-46 to issuance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

Pursuant to 37 CFR § 1.136(a)(3), the Commissioner is hereby authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds, LLP U.S. Deposit Account No. 16-1150 (order no. 011068-029-999).

Respectfully submitted,

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